

Predictors of hospitalization and short-term mortality among lung cancer patients in the emergency department

Lung cancer patients in the emergency department

Yasemin Söyler, Pınar Akın Kabalak, Feza Uğurman
Department of Chest Diseases, Ankara Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

This study was presented as an oral presentation at the 43th annual congress of Türkiye Solunum Araştırmaları Derneği, 2021, Turkey

Abstract

Aim: Lung cancer is one of the leading reasons for emergency department (ED) visits. In this study, we aimed to determine the reasons for ED visits and to identify predictive factors for hospitalization and short-term mortality (30-days mortality).

Material and Methods: We conducted a retrospective, observational study on lung cancer patients admitted to ED of a tertiary hospital between 01 January 2018 and 01 January 2020. Patients' demographic data, main symptoms on admission, laboratory parameters, and radiological findings were recorded. Logistic regression analysis was employed to identify the predictive factors for hospitalization and short-term mortality.

Results: A total of 200 lung cancer patients (174 males, 36 females, mean age 64± 9.5 years) were included in the study. Respiratory symptoms (44.5%), clinical deterioration (23%), and pain (10.5%) were the most common main symptoms; 25% of patients had pneumonia on admission; 53% of patients were hospitalized and 4% of patients died in ED. Among the hospitalized patients, the length of stay in the hospital was 9.5 (1-56) days, during which 48 deaths (41.4%) were recorded. Among all patients, 41% died within 30 days after ED visits. In multivariate logistic regression, the presence of pneumonia was found to be a statistically significant predictive factor in both hospitalization (OR=5.420; 95%CI, 2.114 - 13.898; p < 0.001) and short-term mortality. (OR=0.241; 95%CI, 0.109 - 0.534; p < 0.001).

Discussion: The presence of pneumonia on admission is an important risk factor for hospitalization and short-term mortality. These relationships should be kept in mind for the careful management of lung cancer patients in ED.

Keywords

Emergency Department, Hospitalization, Lung Cancer, Pneumonia, Short-Term Mortality

DOI: 10.4328/ACAM.21119 Received: 2022-02-20 Accepted: 2022-03-23 Published Online: 2022-03-28 Printed: 2022-07-01 Ann Clin Anal Med 2022;13(7):783-787

Corresponding Author: Yasemin Söyler, Kuşcağız Mahallesi, Sanatoryum Cad., 06280, Keçiören, Ankara, Turkey.

E-mail: dryaseminsoyler@gmail.com P: +90 535 843 07 36

Corresponding Author ORCID ID: <https://orcid.org/0000-0002-0507-0767>

Introduction

Lung cancer is a major public health problem worldwide, and almost one-quarter of all cancer deaths are due to lung cancer. Although there is an increase in survival for most cancer types, the 5-year relative survival rate for lung cancer is still low, approximately 21% due to being diagnosed at a distant stage [1,2]. Recent studies have shown that lung cancer is also one of the leading reasons for emergency department (ED) visits due to being a difficult disease to deal with complications related to the tumor itself and the treatment process [3,4]. Symptoms of disease burden or progression, and toxicity associated with anti-cancer treatments may result in ED visits [5]. Some ED visits may be the result of acute onset problems and life-threatening conditions, while some of them are not urgent. For instance, inadequate symptom palliation during routine cancer controls may lead to unnecessary ED visits. These unnecessary visits are likely to become an important problem for the ED system in daily practice. Unfortunately, they are also disturbing and distressful for patients [4]. Moreover, an ED visit is itself an indicator of poor-quality care for patients with cancer and an indicator of poor prognosis [6,7]. It is therefore important to understand why lung cancer patients visit ED and how these visits can be minimized. In this context, we sought to determine the reasons for ED visits and to identify predictive factors for hospitalization and short-term mortality.

Material and Methods

Study design and population

We conducted a retrospective and observational study. Two hundred lung cancer patients over the age of 18 years who visited our hospital's ED between 01 January 2018 and 01 January 2020 were enrolled. If patients had more than one visit, their last ED visit was evaluated. Data were collected from hospital databases and/or patients' files. Patients whose clinical information could not be reached ($n = 6$), patients who refused admission to hospital ($n = 7$), patients who were transferred to another hospital ($n = 4$) and patients who had a cancer other than lung cancer ($n = 9$) were excluded from the study (Figure 1).

Patients' demographic features like age, sex, comorbid diseases, presence of chronic obstructive pulmonary disease (COPD), routine laboratory parameters, presence of pneumonia and cancer status (clinical stage, histological type, metastasis site, type of cancer treatment) were collected. The clinical stage was classified as early stage for TNM I-II, locally advanced stage for TNM IIIA-B-C and advanced stage for TNM IV [8]. The presenting symptom, which was defined as the main symptom causing the visit to ED, was evaluated. These symptoms were grouped as respiratory (dyspnea, cough, sputum, chest pain and hemoptysis), gastrointestinal (nausea, vomiting, diarrhoea/constipation, abdominal pain, a decrease in spontaneous food intake and bleeding), neurological (dizziness, headache, emotional problems, and loss of consciousness), clinical deterioration, pain and fever. Patient outcomes after initial assessment (discharged from ED, hospitalized from ED, died in ED) were recorded. If a patient was hospitalized length of stay in the hospital and patient outcomes after hospitalization (discharged from hospital, died in hospital) were also recorded.

The predictive factors for hospitalization and short-term mortality (mortality rate within 30 days after ED visit) were evaluated with univariate and multivariate analyses.

This study was approved by the medical specialty education board of our centre [(Decision no: 643, Date: 19.09.2019 and Decision no:19, Date: 06.01.2022 (readjustment))] and was performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was waived because of the retrospective nature of the study.

Statistical Analyses

SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc. was used for the database and statistical analyses. Baseline characteristics of study were generated using frequency and descriptive analyses. Continuous data were described as mean \pm standard deviation (SD) for normal distributions, and median (minimum – maximum value) for skewed distribution and categorical variables, expressed as either frequency (percentage) Chi square was used to compare non-parametric factors between groups. For parametric variables, Student's t-test or variance analyses were used. To determine where the differences originated from, post-hoc analysis and Bonferroni correction have been applied. The short-term mortality was calculated using life-tables. Multivariate logistic regression analysis was employed to identify the predictive factors for hospitalization and short-term mortality by performing stepwise variable selection on those variables with a univariate p -value < 0.05 . Odds ratios (ORs) were calculated with 95% confidence intervals (95% CI). Any p -value < 0.05 was considered significant.

Results

A total of 200 lung cancer patients (174 males, 36 females, mean age 64 ± 9.5 years) were included in the study. A majority of patients ($n = 128$, 64%) had at least one comorbid disease, and chronic obstructive lung disease (COPD) was accompanied

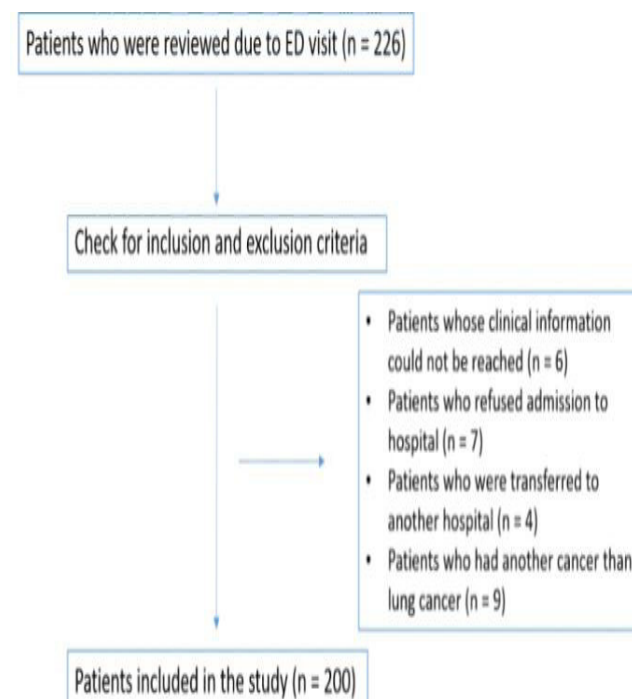


Figure 1. The flow chart of the study population

in 36% (n = 72) of patients. Pneumonia was present in 25% (n = 50) of patients on admission. The most frequent histological type was squamous cell carcinoma (n = 87, 43.5 %) and the most frequent stage was advanced stage (n = 106, 53%). The most applied treatment type was chemotherapy/tyrosine kinase inhibitors (TKIs) (n = 70, 35%), followed by best supportive care (BSC) (n = 63, 31.5%). Respiratory symptoms (n = 89, 44.5%), clinical deterioration (n = 46, 23%), and pain (n = 21, 10.5%) were the most common main symptoms (Table 1).

The treatment of 76 (38%) patients was completed in ED and they were discharged. One hundred and sixteen (53%) patients were hospitalized from ED, and 8 (4%) patients died in ED. Demographic, clinical characteristics and laboratory parameters according to patients' outcomes after initial assessment (discharged from ED, hospitalized from ED and died in ED) were compared (Table 2). According to post-hoc analysis and Bonferroni correction, CRP (p < 0.001), stage (p = 0.004), existence of comorbidity (p = 0.025) and presence of pneumonia (p < 0.001) were significantly associated with outcomes after initial assessment.

The mean length of stay in hospital was 9.5 (1 – 56) days, during which 48 deaths (41.4%) were recorded. Comparison of demographic, clinical characteristics and laboratory parameters of hospitalized patients [(discharged from hospital (n = 68, 58.6%), died in hospital (n = 48, 41.4%)] is shown in Table 3.

Based on the univariate regression analyses, the existence of

Table 1. The baseline demographic and clinical characteristics of study population

Variables	Number of patients (n, %)
Age, years (mean ± SD)	64 ± 9.5
Sex (Male / Female)	174 / 26
Existence of comorbidity	124 (64%)
Presence of COPD	72 (36%)
Presence of pneumonia	50 (25%)
Histological subtype	
SCLC / Adenocarcinoma / SCC	40 (20%) / 73 (36.3%) / 87 (43.5)
Clinical stage	
Early / Locally advanced / Advanced	27 (13.5%) / 67 (33.5%) / 106 (53%)
Treatment types	
Chemotherapy / TKIs	70 (35%)
Chemo-radiotherapy	11 (5.5%)
Extra thoracic radiology	15 (7.5%)
Best supportive care	63 (31.5%)
Follow-up	41 (20.5%)
Presenting symptom	
Respiratory symptoms	89 (44.5%)
Clinical deterioration	46 (23%)
Pain	21 (10.5%)
Gastrointestinal symptoms	18 (9%)
Neurological symptoms	17 (8.5%)
Fever	9 (4.5%)
Laboratory findings	
White blood cell count (median, min-max)	10360 (2340 – 36120)
Neutrophil count (median, min-max)	8255 (3– 34850)
C-reactive protein (mean ± SD)	113.1 ± 98.2
Length of stay in hospital (median, min-max)	9.5 (1-56)

Abbreviations: SD, Standard deviation; COPD, Chronic obstructive pulmonary disease; SCC, Squamous cell carcinoma; SCLC, Small cell lung cancer; TKIs, tyrosine kinase inhibitors

comorbidity, the presence of COPD, the presence of pneumonia, histological type of tumor, clinical stage, the presence of cranial metastasis and increased CRP levels were found to be statistically significant predictive factors for hospitalization. In the multivariate logistic regression, the presence of pneumonia (OR = 5.420; 95% CI, 2.114 – 13.898; p < 0.001), histological type of tumour (OR = 1.951; 95% CI, 1.223 – 3.114; p = 0.005) and increased CRP levels (OR = 1.005; 95% CI, 1.001 – 1.008; p = 0.016) were found to be statistically significant predictive factors for hospitalizations.

Among all patients, eighty-two (41%) of them died within 30 days after ED visits. Based on univariate regression analyses, the presence of pneumonia, clinical stage, presenting symptom, the presence of cranial metastasis and the presence of bone metastasis were found to be statistically significant predictive factors for short-term mortality. In the multivariate logistic regression, the presence of pneumonia was found to be a statistically significant predictive factor for the short-term mortality (OR = 0.241; 95% CI, 0.109 - 0.534; p < 0.001).

Discussion

Lung cancer patients frequently visit EDs from the beginning of the diagnostic process till the end of their lives for cancer related or unrelated reasons. Although ED visits have a negative effect the system, it would be inappropriate to expect this situation to disappear completely [4]. For this reason, clinicians should determine reasons, focus on the management of symptoms and minimise the number of visits at least. According to our study, the most common main symptoms are respiratory symptoms, clinical deterioration, and pain. Importantly, the presence of pneumonia is the predictive factor for both hospitalization, and short-term mortality.

As expected, the most common symptoms are respiratory symptoms, suggesting that clinicians should question respiratory symptoms more thoroughly at routine cancer controls and properly administer antibiotics, corticosteroids, bronchodilator therapies, long-term oxygen therapy, or non-invasive mechanical ventilation if necessary [3,9–12]. Clinical deterioration, also defined as alteration of general state, poor clinical condition, poor performance status or deteriorated general health, was the second reason for ED visits in our study. This is a general term that can be associated with hypoxia, infections, fluid and electrolyte disorders, dehydration, cachexia, metastasis, fatigue or weakness [9]. It is also common in patients who received chemotherapy, suggesting that the side effects of the treatment may cause this. In addition, patients with locally advanced and advanced stages, possibly related to the natural course of cancer, are mostly presented with clinical deterioration [3,9–12]. The high number of advanced-stage patients or the high number of patients receiving chemotherapy is likely to be the reason for the frequent occurrence of clinical deterioration in our study. To avoid unnecessary ED visits, adequate information about the natural course of cancer, and education about appropriate symptom management and treatment side effects are important issues. Thereby, patients and their caregivers could be prepared for expected problems and could solve some of them at their homes instead of EDs. ED visits could be reduced through these approaches and also

Table 2. Comparison of data according to outcomes after initial assessment

Variables	Discharged from ED (n = 76)	Hospitalized from ED (n = 116)	Died in ED (n = 8)	p value
Age, years (mean ± SD)	62 ± 9.5	64.4 ± 9.4	67.7 ± 8.5	0.104
Existence of comorbidity	38	88	6	0.031
Presence of COPD	23	48	1	0.108
Presence of pneumonia	6	43	1	<0.001
Histological subtype				0.034
SCLC / Adenocarcinoma / SCC	19/32/25	18/41/57	3/0/5	
Clinical stage				0.008
Early / Locally advanced / Advanced	18/26/32	8/40/68	1/1/6	
Treatment types				0.219
Chemotherapy / TKIs	30	38	2	
Chemo-radiotherapy	7	4	0	
Extra thoracic radiology	4	10	1	
Best supportive care	16	44	3	
Follow-up	9	20	2	
Presenting symptom				0.013
Respiratory symptoms	35	49	5	
Clinical deterioration	7	36	3	
Pain	13	8	0	
Gastrointestinal symptoms	11	7	0	
Neurological symptoms	7	10	0	
Fever	3	6	0	
Laboratory findings				
WBC count (x10 ⁹ , median,min-max)	9.1(0.7-41)	10.7(0.2-36)	24(11-65)	<0.001
Neutrophil count (x10 ⁹ , mean ± SD)	6.8 ± 5.3	8.8 ± 6.2	19.8 ± 17	<0.001
C-reactive protein (mean ± SD)	65.2 ± 81.1	139.2 ± 97.5	193 ± 64	<0.001

Abbreviations: COPD, Chronic obstructive pulmonary disease; SCC, Squamous cell carcinoma; SCLC, Small cell lung cancer; TKIs, tyrosine kinase inhibitors

Table 3. Comparison of data according to outcomes after hospitalization

Variables	Discharge from hospital (n = 68)	Death in hospital (n =48)	p value
Age, years (mean ± SD)	65 ± 9.4	63.6 ± 9.5	0.41
Existence of comorbidity	47	37	0.052
Presence of COPD	32	16	0.053
Presence of pneumonia	17	26	<0.001
Clinical stage			<0.001
Early / Locally advanced / Advanced	8 / 30 / 30	0 / 10 / 38	
Histological type			0.51
SCLC / Adenocarcinoma / SCC	9 / 20 / 39	9 / 21 / 18	
Treatment types			0.001
Chemotherapy/TKIs	24	14	
Chemo-radiotherapy	4	0	
Extra thoracic radiotherapy	7	3	
Best supportive care	16	28	
Follow-up	17	3	
Presenting symptom			0.001
Respiratory symptoms	33	16	
Clinical deterioration	14	22	
Pain	5	3	
Gastrointestinal symptoms	5	2	
Neurological symptoms	5	5	
Fever	6	0	
WBC count (x10 ⁹ ,mean ± SD)	9.3 ± 6.3	12.8 ± 6.6	0.005
Neutrophil count (x10 ⁹ ,mean ±SD)	7.4 ± 5.9	10.7 ± 6.1	0.005
C-reactive protein (mean ± SD)	120 ± 92.8	165 ± 98.8	0.014
Brain metastasis	12	17	0.001
Bone metastasis	15	19	0.048

Abbreviations: COPD, Chronic obstructive pulmonary disease; SCC, Squamous cell carcinoma; SCLC, Small cell lung cancer; TKIs, tyrosine kinase inhibitors

substantial palliative care [7,10]. Pain is the other common reason for ED visits in our study in line with previous studies [3,9–12]. As known, pain management needs to begin as soon as possible, since uncontrolled pain can cause frequent ED visits, and comprehensive pain management with the patient's primary care physician or pain specialist may reduce ED visits related to this symptom [13–15].

Identifying risk factors for hospitalization and mortality after ED visit is important to be more cautious to these patients, and to inform patients and their caregivers. Previous studies have revealed that the rate of hospitalization, ICU requirement and mortality after ED visits was higher in patients with lung cancer [9,11,12,16,17]. Consistent with these studies, 58% of patients hospitalized from ED, and 41% of patients died within 30 days in our study. A previous study also showed that arrival type and time, known lung disease, clinical deterioration, senility, and having bradycardia or tachycardia were independent predictors for hospitalization [12]. Another study, which was related to advanced cancer patients, has found that the presence of lung tumor, the presence of respiratory and neurological symptoms, icterus and high levels of calcium were risk factors for death after ED visits [10]. In our study, the histological type of tumor and increased CRP levels were found to be independent predictive factors for hospitalization. It cannot be ruled out that the higher number of patients with squamous cell carcinoma may have influenced this result. Moreover, the presence of pneumonia is found to be an independent predictive factor for both hospitalization and short-term mortality in our study. It should be noted that pneumonia is a common disease and results in high fatality. Patients are likely to require more frequent ED visits because both cancer and pneumonia may worsen clinical conditions [3]. Given these issues, it is not surprising that hospitalization and death are frequent in lung cancer patients with pneumonia.

Our study has several limitations. This is a retrospective and single-center study, which was conducted in a chest diseases hospital with staff experienced in lung cancer and oncological emergencies. Thus, it may be difficult to generalize our results to ED of general hospitals. Although we classified patients according to their main symptoms on the basis of reviewing their medical records, it is possible that two or more main symptoms coexisted in some cases. Additionally, there are differences in request for place of death (home/hospital) between patients/caregivers. Thus, this could affect outcome results.

Conclusions

Our findings showed that lung cancer patients frequently visit ED due to respiratory symptoms, clinical deterioration and pain. Moreover, the presence of pneumonia on admission is an important risk factor for hospitalization and short-term mortality. These relationships should be kept in mind for the careful management of lung cancer patients in ED.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with

the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:

Yasemin Söyler, Pınar Akın Kabalak, Feza Uğurman. Predictors of hospitalization and short-term mortality among lung cancer patients in the emergency department. *Ann Clin Anal Med* 2022;13(7):783–787